Amendments to the claims:

This listing of claims replaces all prior versions

Listing of Claims:

1. (Currently amended) A method of identifying a compound that modulates JNK3 expression, the method comprising:

incubating a neuronal cell that can express a JNK3 protein with a test compound under conditions and for a time sufficient for the cell to express a JNK3 protein absent the test compound, wherein the compound is a peptide, a peptidomimetic, a small organic molecule, or a small inorganic molecule;

incubating a control cell under the same conditions and for the same time absent the test compound;

measuring JNK3 expression in the cell in the presence of the test compound;

measuring JNK3 expression in the control cell; and

comparing the amount of JNK3 expression in the presence and absence of the test compound, wherein a difference in the level of expression indicates that the compound modulates JNK3 expression.

2. (Currently amended) The method of claim 1, wherein the test compound decreases the expression of JNK3.

3-6. Canceled

7. (Withdrawn) A method for generating a totipotent mouse cell comprising at least one inactivated JNK3 gene, the method comprising:

a. providing a plurality of totipotent mouse cells;

b. introducing into the cells a DNA construct comprising a disrupted mouse JNK3 gene, wherein the JNK3 gene is disrupted by insertion of a nucleotide sequence into the gene that prevents expression of functional JNK3;

c. incubating the cells such that homologous recombination occurs between the chromosomal sequence encoding JNK3 and the introduced DNA construct; and

d. identifying a totipotent mouse cell comprising at least one inactivated JNK gene.

8. (Withdrawn) A method for generating a mouse homozygous for an inactivated JNK3 gene comprising:

a. providing a totipotent mouse cell comprising at least one inactivated JNK3 gene;

b. inserting the cell into a mouse embryo and implanting the embryo into a female mouse;

c. permitting the embryo to develop into a neonatal mouse;

d. permitting the neonatal mouse to reach sexual maturity; and

e. mating two sexually mature mice of step d.

to obtain a mouse homozygous for the inactivated JNK3 gene(-/-), wherein the homozygous JNK3(-/-) mouse is resistant to excitotoxic damage.

9. (Withdrawn) A method of treating a patient having or at risk for a disorder involving excitotoxicity, the method comprising administering to the patient a therapeutically effective amount of a compound that inhibits JNK3 expression.

10. (Withdrawn) The method of claim 9, wherein the compound is an antisense nucleic acid molecule.

11. (Withdrawn) The method of claim 9, wherein the disorder is selected from the group consisting of Alzheimer's disease, Huntington disease, ischemia, amyotrophic lateral sclerosis, trauma, motorneuron disease, Parkinson's disease, or epilepsy.

12. (Withdrawn) A transgenic non-human mammal having a transgene disrupting expression of a JNK3 gene, the transgene being chromosomally integrated into germ cells of the mammal.

13. (Withdrawn) The mammal of claim 12, wherein the mammal is a mouse.

14. (Withdrawn) The mammal of claim 12, wherein the germ cells are homozygous for the transgene.

15. (Withdrawn) The mammal of claim 12, wherein the disruption results in a null mutation.

16. (Withdrawn) A cell line descended from a cell of the mammal of claim 12.

17. (Withdrawn) A DNA construct comprising a disrupted mouse JNK3 gene, including an insertion of a nucleotide sequence into the gene that prevents or modifies the expression of functional JNK3.

18. (Previously presented) The method of claim 1, wherein the compound is a soluble peptide.

19. (Previously presented) The method of claim 1, wherein the compound is a phosphopeptide.

20.-22. (Canceled )

23. (Currently amended) A method of identifying whether a test compound ~~a compound that~~ modulates JNK3 expression, the method comprising:

incubating a cell that can express a JNK3 protein with a test compound under conditions and for a time sufficient for the cell to express a JNK3 protein absent the test compound;

incubating a control cell under the same conditions and for the same time absent the test compound;

measuring JNK3 expression in the cell in the presence of the test compound;

measuring JNK3 expression in the control cell;

comparing the amount of JNK3 expression in the presence and absence of the test compound;

selecting the test compound if there is a difference in the level of expression in the presence and absence of the test compound; and

administering the selected compound to an animal model of an excitotoxic disorder and assaying the animal for excitotoxicity,

wherein a decrease in excitotoxicity in the animal indicates that the test compound modulates JNK3 expression.

24. (Currently amended) The method of claim 23, wherein the test compound decreases the expression of JNK3.

25. (Previously presented) The method of claim 23, wherein the animal model is a mouse model.

26. (Previously presented) The method of claim 23, wherein the excitotoxic disorder is kainic acid-induced or pentetrazole-induced.

27. (Currently amended) A method of identifying whether a test compound ~~a compound that~~ modulates JNK3 activity, the method comprising:

incubating a cell that exhibits JNK3 activity with a test compound under conditions and for a time sufficient for the cell to exhibit JNK3 activity absent the test compound;

incubating a control cell under the same conditions and for the same time absent the test compound;

measuring JNK3 activity in the cell in the presence of the test compound;

measuring JNK3 activity in the control cell;

comparing the amount of JNK3 activity in the presence and absence of the test compound;

selecting the test compound if there is a difference in the level of activity in the presence and absence of the test compound; and

administering the selected test compound to an animal model of an excitotoxic disorder and assaying the animal for excitotoxicity, wherein a decrease in excitotoxicity in the animal indicates that the test compound modulates JNK3 activity.

28. (Previously presented) The method of claim 27, wherein the animal model is a mouse model.

29. (Previously presented) The method of claim 27, wherein the excitotoxic disorder is kainic acid-induced or pentetrazole-induced.

30. (Currently amended) The method of claim 27, wherein the test compound decreases JNK3 activity.

31. (Currently amended) The method of claim 27, wherein the test compound is a peptide, a peptidomimetic, a small organic molecule, a small inorganic molecule, or an oligonucleotide.

32. (Currently amended) A method of identifying whether a test compound ~~a compound that~~ modulates the binding of a JNK3 polypeptide to a substrate, the method comprising:

comparing the amount of a JNK3 polypeptide bound to a substrate in the presence and absence of a test compound;

selecting the test compound if there is a difference in the amount of JNK3 polypeptide bound to the substrate in the presence and absence of the test compound; and

administering the selected test compound to an animal model of an excitotoxic disorder and assaying the animal for excitotoxicity,

wherein a decrease in excitotoxicity in the animal indicates that the selected compound modulates the binding of a JNK3 polypeptide to the substrate.

33. (Previously presented) The method of claim 32, wherein the animal model is a mouse model.

34. (Previously presented) The method of claim 32, wherein the excitotoxic disorder is kainic acid-induced or pentetrazole-induced.

35. (Previously presented) The method of claim 32, wherein the binding of a JNK3 polypeptide to a substrate is decreased.

36. (Previously presented) The method of claim 32, wherein the test compound is a peptide, a peptidomimetic, a small organic molecule, a small inorganic molecule, or an oligonucleotide.

37-45. (Canceled)

46. (Currently amended) A method of determining whether a test compound ~~identifying a compound that~~ inhibits phosphorylation of a JNK3 substrate, the method comprising:

comparing the amount of a JNK3 substrate phosphorylated in the presence compared to the absence of a test compound;

selecting the test compound if there is a decrease in the amount of JNK3 substrate phosphorylation in the presence of the test compound compared to phosphorylation in the absence of the test compound; and

administering the selected test compound to an animal model of an excitotoxic disorder to assess excitotoxicity,

wherein a decrease in excitotoxicity indicates that the selected test compound inhibits the phosphorylation of a JNK3 substrate.

47. (Previously presented) The method of claim 46, wherein the JNK3 substrate is c-Jun.

48. (Previously presented) The method of claim 23, wherein the test compound is a peptide, a peptidomimetic, a small organic molecule, or a small inorganic molecule.

49. (Previously presented) A method of identifying a candidate compound for the treatment of a disorder related to excitotoxicity, the method comprising:

incubating a neuronal cell that can express a JNK3 protein with a compound under conditions sufficient to express the JNK3 protein;

incubating a control cell under the same conditions and for same time absent the compound; and

comparing the level of JNK3 activity in the presence and absence of the compound, wherein a difference in the level of JNK3 activity indicates that the compound is a candidate compound for the treatment of a disorder related to excitotoxicity.

50. (Previously Presented) A method of identifying a candidate compound for the treatment of a disorder related to excitotoxicity, the method comprising:

incubating a JNK3 protein expressed and isolated from a neuronal cell with a JNK3 substrate and a compound under conditions sufficient to allow the interaction of the JNK3 protein with a JNK3 substrate;

incubating the JNK3 protein and the JNK3 substrate under the same conditions and for the same time absent the compound; and

comparing the level of JNK3 activity in the presence and absence of the compound, wherein a difference in the level of JNK3 activity indicates that the compound is a candidate compound for the treatment of a disorder related to excitotoxicity.

51. (Previously Presented) A method of identifying a candidate compound for the treatment of a neuronal disorder, the method comprising:

incubating a JNK3 protein expressed and isolated from a neuronal cell with a JNK3 substrate and a compound under conditions sufficient to allow the interaction of the JNK3 protein with the JNK3 substrate;

incubating the JNK3 protein and the JNK3 substrate under the same conditions and for same time absent the compound; and

comparing the level of JNK3 activity in the presence and absence of the compound, wherein a difference in the level of JNK3 activity indicates that the compound is a candidate compound for the treatment of a neuronal disorder.

52. (Previously Presented) A method of identifying a candidate compound for the treatment of a neuronal disorder, the method comprising:

incubating a neuronal cell that can express a JNK3 protein with a compound under conditions sufficient to express the JNK3 protein;

incubating a control cell under the same conditions and for same time absent the compound; and

comparing the level of JNK3 activity in the presence and absence of the compound, wherein a difference in the level of JNK3 activity indicates that the compound is a candidate compound for the treatment of a neuronal disorder.

53. (Previously presented) The method of claim 49, 50, 51, or 52, wherein the compound is a peptide, a peptidomimetic, a small organic molecule, or a small inorganic molecule.

54. (Previously presented) The method of claim 49, 50, 51, or 52, wherein the compound inhibits the ability of JNK3 to phosphorylate a substrate.

55. (Previously presented) The method of claim 54, wherein the substrate is c-Jun.

56. (Previously presented) The method of claim 49, 50, 51, or 52, wherein the compound inhibits the ability of JNK3 to bind a substrate.

57. (Previously presented) The method of claim 56, wherein the substrate is c-Jun.

58. (Previously presented) The method of claim 49 or 50, wherein the excitotoxic disorder is kainic acid-induced or pentetrazole-induced.

59. (Previously presented) The method of claim 49, 50, 51, or 52, wherein the disorder is a seizure disorder, epilepsy, cerebrovascular disorder, ischemia, spinal cord injury, spinal cord pressure, dementia, Alzheimer's disease, Parkinson's disease, a neurogenerative disorder, Huntington disease, or motoneuron disease.

60. (New) A method of identifying a compound that modulates JNK3 expression, the method comprising

a) incubating a cell that can exhibit excitotoxicity and can express a JNK3 protein with a compound under conditions and for a time sufficient for the cell to express a JNK3 protein absent the compound;

b) incubating a control cell under the same conditions as in step (a) and for the same time absent the compound;

c) measuring excitotoxicity in the cell in the presence of the compound;

d) measuring excitotoxicity in the control cell; and

e) comparing the amount of excitotoxicity in the presence and absence of the compound, wherein a difference in the level of excitotoxicity indicates that the compound modulates JNK3 expression.

61. (New) A method of claim 60, wherein the compound decreases the expression of JNK3.

62. (New) The method of claim 60, wherein the compound decreases excitotoxicity.

63. (New) A method of identifying a compound that modulates JNK3 excitotoxicity, the method comprising

a) incubating a cell that can exhibit excitotoxicity under conditions and for a time sufficient for the cell to express excitotoxicity in the absence of the compound;

b) incubating a control cell for the same time and under the same conditions in the absence of the compound;

c) measuring excitotoxicity in the cell in the presence of the compound;

d) measuring excitotoxicity in the control cell; and

e) comparing the amount of excitotoxicity in the presence and absence of the compound, wherein a difference in the level of excitotoxicity indicates that the compound modulates excitotoxicity.

64. (New) A method of claim 63, wherein the compound decreases excitotoxicity.

65. (New) A method according to any one of the claims 60 to 64, wherein the compound is a soluble peptide.

66. (New) A method according to any one of the claims 60 to 64, wherein the compound is a phosphopeptide.

67. (New) A method according to any one of the claims 60 to 64, wherein the compound is a peptidomimetic.

68. (New) A method according to any one of the claims 60 to 64, wherein the compound is a small organic molecule.

69. (New) A method according to any one of the claims 60 to 64, wherein the compound is an inorganic molecule.